VICH International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

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STEP 2 DOCUMENT

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: Residual Moisture Test

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VICH, International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products

WORKING GROUP: Biologicals Quality Monitoring

TOPIC: Test for Residual Moisture

GUIDELINE

FOR TESTING OF

RESIDUAL MOISTURE

(v3.1)

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INTRODUCTION

1) Objective of Guideline

Freeze-dried veterinary vaccines always contain some water, commonly known as residual moisture (RM). It is important to determine the level of RM in final products, since a satisfactory test gives assurance of an adequate shelf life and that the manufacturer's freeze-dry cycle was properly controlled. The RM test should confirm that moisture level is consistently within the manufacturer's specification.

This document provides a guideline on the general requirements for residual moisture testing. The guideline leaves the flexibility for other test methods based on the specific scientific situations or characteristics of the target material. These variations must be stated in the manufacturer's production method and include equivalence data. It is recognized that the limits for the alternative equivalent assay may be different from the gravimetric assay.

2) Scope of Guideline

This guideline applies to final product testing for all freeze-dried veterinary vaccines.

3) Background

Three common methods are generally recognized for use in determining residual moisture, these are:

- Titrimetric method, (Karl Fischer)
- Azeotropic method
- Gravimetric method.

Neither EU or USDA specify a test for residual moisture. The USA Code of Federal Regulations (9CFR 113.29) states " a suitable method used to determine the moisture content shall be described in an outline of production approved for filing by APHIS." The EU Directives/Guidelines state that each batch <of product> is tested for residual humidity and " Where applicable, the freeze-drying process is checked by a determination of water and shown to be within the limits set for the product." Japanese Standard Requirements specify the "loss on drying method."

4) General Principle

Residual moisture is determined by the gravimetric method as follows: Residual moisture is driven from the test product by heating under vacuum. The residual moisture content (as per cent) of the test product is calculated based the product weight loss during the drying cycle.

Residual Moisture Assay

1. Materials and equipment

1.1 Cylindrical weighing bottles--individually numbered with airtight glass stoppers.
1.2 Vacuum oven--equipped with validated thermometer and thermostat. A suitable air-drying device must be attached to the inlet valve.
1.3 Balance--capable of readability to 0.1 mg (rated precision ± 0.1 mg).
1.4 Desiccator--with phosphorus pentoxide, silica gel or equivalent
1.5 Sample--desiccated veterinary vaccine in original sealed vial.

2. Preparation for the test

2.1 Preparation for the test – Environment
Conduct all operations in an environment with a relative humidity less than 45%.

2.2 Preparation for the test – Weighing bottles
Label the weighing bottle for sample(s). Thoroughly clean weighing bottles. Place stopper at an angle on top of bottle and dry for a minimum of 30 minutes at 60° ± 3°C under vacuum (<2.5 kPa). While hot, immediately transfer bottles and stoppers into a desiccator. Allow to cool to room temperature, close stopper, weigh and record the weights as “A”. Return bottles to desiccator.

2.3 Preparation of the sample and the control
Retain sample and control, in original airtight containers at room temperature until use. Do not break the seal until ready to proceed.

3. Performance of the test

3.1 Procedure

3.1.1 Break sample container seal. Using a spatula, break up desiccated product and rapidly transfer (minimum of 100 mg, 50 mg for single dose products, use more than one vial for single dose products if needed) to a previously weighed bottle. Close stopper and immediately weigh. Record the weight as “B”.

3.1.2 Place the bottle with the stopper at an angle in the vacuum oven. Set vacuum to <2.5 kPa and the temperature to 60° ± 3°C.

3.1.3 After a minimum of 3 hrs, turn off the vacuum pump and bleed dry air into the oven until the pressure inside of the oven is equalized with the atmosphere.

3.1.4 While the bottle is still warm, stopper bottle and transfer to desiccator, and allow to cool to room temperature (for a minimum of two hours or a time validated to yield a constant weight). Weigh, and record the weight as “C”.

3.2 Calculations

Record weights
A is tare weight of bottle.
B minus A is weight of sample before assay.
B minus C is weight equivalent to residual moisture of sample.
Then ((B - C) / (B - A)) X (100) = % of residual moisture.

4. Results

Results are considered satisfactory if the per cent residual moisture is less than or equal to the manufacturer's specification.